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**Basic requirements
for cancer screening recommendations
based on insufficient evidence**
~Comparison of guidelines in Korea and Japan~



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Objective

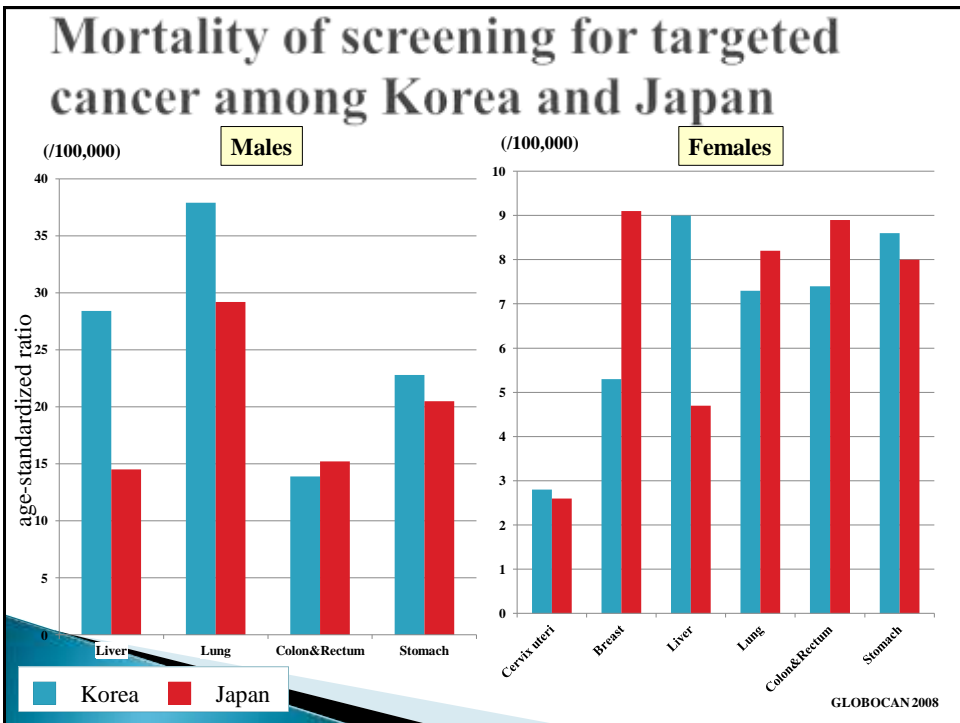
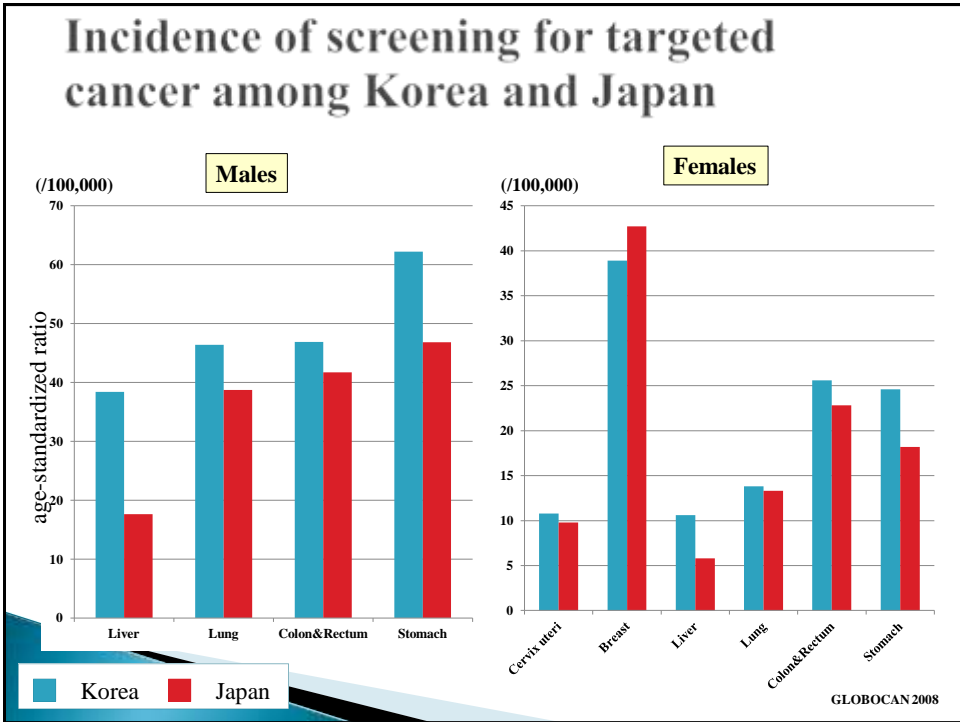
- ▶ When deciding to make recommendations, the local situation and evidence should be considered.
- ▶ We compared the cancer screening guidelines in Korea and Japan to clarify the basic requirements for recommendations based on insufficient evidence.

Comparison between Korean and Japanese Guidelines for Cancer Screening

Korea			Cancer Screening	Japan		
Method	Target	Interval		Method	Target	Interval
Endoscopy or UGI	≥40 yrs	2 yrs	Stomach	UGI	≥40 yrs	1 yr
FOBT	≥40 yrs	1 yr	Colon& Rectum	FOBT	≥40 yrs	1 yr
-	-	-	Lung	Chest XP + sputum cytology (current smoker)	≥40 yrs	1 yr
Ultrasography +AFP	≥40 yrs (high-risk group)	6 m	Liver	HBV antigen + HCV antibody	≥40 yrs	1 time /life year
MMG+PE	≥40 yrs	2 yrs	Breast	MMG+PE	≥40 yrs	2 yrs
Pap smear	≥30 yrs	2 yrs	Cervix	Pap smear	≥20 yrs	2 yrs

Methods

- ▶ The following items were compared between Korea and Japan to determine recommendations for cancer screening: all evidence for recommendations, original studies, disease burden and other factors.
- ▶ Additional literatures were identified by searching MEDLINE after the guidelines were published in Japan.



Comparison of Evidence between Korean and Japanese Guidelines

Cancer	Publication of Japanese guidelines	Method	Before		After	
			RCT	Observational studies	RCT	Observational studies
Stomach	2005	Radiography	0	7	0	3
		Endoscopy	0	1	0	2
Lung	2006	Radiography	4	5	0	0
Hepatitis	2010	HBV antigen	0	0	0	0
		HCV antibody	0	0	0	0
Heaptocellular carcinoma	2010	Ultrasonography + AFP	1	1	0	1

Case-Control Studies of Radiographic Screening for Gastric Cancer

Author	Reported year	Age	No of subjects	Odds ratio (95%CI) *90%CI **99%CI
Oshima A	1986	≥40 yrs	Males: 54 cases/ 156 controls Females: 37 cases/ 105 controls	Males: 0.595(0.338-1.045)* Females: 0.382(0.185-0.785)*
Pisani P	1994	≥35yrs	All: 85 cases/ 375 controls	All: 0.47(0.24-0.98) All: 0.25(0.12-0.51)
Fukao A	1995	≥50yrs	Males: 126 cases/ 364 controls Females: 72 cases/ 213 controls	Males: 0.32(0.19-0.53) Females: 0.63(0.34-1.16)
Abe Y	1995	30-89yrs	Males: 527 cases /1,552 controls Females: 293 cases / 861 controls	Males: 0.371(0.242-0.568)** Females: 0.458(0.263-0.797)**
Tsubono Y	1999	40-64yrs	All: 27 cases/ 270 controls	All:0.20(0.04-0.96)
Tsubono Y (meta-analysis)	1999	-	Males: 706 cases/2,072 controls Females: 402 cases/ 1,179 controls	Males: 0.39(0.29-0.52) Females: 0.50(0.34-0.71)

Evidence for Endoscopic Screening for Gastric Cancer

Author	Reported year	Study design	Follow-up	Target age	No of subjects	Outcomes
Rieken B	2002	Case-series	4 years	35-64yrs	4,394	SMR(95%CI) 1.01 (0.72-1.37)
Matsumoto S	2007	Before-after	Before (XP) 7 years After (GFS) 10 years	≥40 yrs	before:4,261 after:7,178	SMR(95%CI) Before:males1.04(0.50-1.58) female s1.54(0.71-2.38) After: males 0.71(0.33-1.10) females 0.62(0.19-1.05)
Hosokawa O	2008	Cohort	10 years	40-74 yrs	GFS screened:2,192 no screened:9,571	Relative risk (95%CI) all:0.3465(0.1365-0.8604) males:0.2174(0.0676-0.6992) females:0.6835(0.1595-2.9286)

Evidence for Lung Cancer Screening

- ▶ For evaluation of chest radiography and its use in combination with sputum cytology, 4 randomized controlled trials (RCTs) and 5 case-control studies were found.
- ▶ All RCTs were conducted in the 1970s and 1980s. These results did not suggest that lung cancer screening reduced mortality.
- ▶ However, treatment for lung cancer has been improved since these studies were conducted. Mortality reduction from lung cancer was shown in 4 of 5 case-control studies conducted after the late 1990s in Japan.

Is it sufficient to evaluate the efficacy of cancer screening based only on observational studies?

- ▶ **Many guidelines recommend cervical cancer screening based on the results of observational studies due to a lack of evidence obtained from RCTs.**
- ▶ **In Japan, gastric, lung and colorectal cancer have been leading causes of cancer deaths. Cancer screening programs to prevent these cancers are thus required.**
- ▶ **However, no RCTs in Japan have dealt with cancer screening. Case-control studies have been conducted to evaluate screening programs for gastric, lung, cervical, and colorectal cancer.**
- ▶ **Several studies have compared the results based on RCTs and observational studies and have reported similar estimates of the effects (Concato et al. NEJM ;Benson et al. NEJM. 2000)**
- ▶ **Recommendation based on the GRADE system could be defined based on not only study design, but also other factors as follows; balance between desirable and undesirable effects: values and preferences: and costs (resource allocations).**

Evidence for Screening for Hepatitis B and C Infection

▶ **Hepatitis B infection**

Several studies, including RCTs, evaluated reduction of liver cirrhosis and hepatocellular carcinoma by antiviral therapy using interferon and nucleoside analogs. However, there is no evidence to evaluate reduction of mortality from hepatitis B-related disease by screening for hepatitis B infection.

▶ **Hepatitis C infection**

Although the chain of evidence suggests the efficacy of screening for hepatitis C infection, there is no direct evidence to evaluate reduction of mortality from hepatitis C-related disease.

Evidence for Ultrasonographic Screening for Hepatocellular Carcinoma

Author	Study design	Published year	Country	Screening method	Number of study group	Target group	Target age	Male(%)	Follow-up years	Outcome	Results
Zhang BH	RCT	2004	China	US+AFP every 6 months	Intervention 9,373 Control 9,443	HBsAg positive or chronic hepatitis	35-59 years	Intervention 62.6% Control 63.3%	5	Incidence Mortality	1.37 0.63 (0.41-0.98)
Chen TH	Cohort study	2002	Taiwan	US	Screening 4,385 No screening 458	HBsAg positive HCAb positive abnormal AFP abnormal liver function family history	≥50yrs screening 45.0% no screening 43.3%	Screening 78.7% No screening 59.8%	7	Mortality	0.76 (0.38-1.52)

Results

▶ Gastric cancer screening

In Japanese guidelines, radiographic screening was recommended based on observational studies mainly conducted in Japan. The efficacy of endoscopic screening is still unclear.

▶ Lung cancer screening

Although the disease burden of lung cancer is heavy in Korea and Japan, the Korean guideline was not recommend lung cancer screening. However, in the Japanese guidelines, lung cancer screening was recommended based on observational studies mainly conducted in Japan.

▶ Screening for hepatitis-related disease

Although the disease burden of hepatitis-related disease is heavy in Korea and Japan, evidence of screening hepatitis-related disease is still insufficient.

Balance of Evidence and Local Situation

- ▶ Cancer screening has been expected to decrease disease burden. Thus, some cancer screening has been performed despite insufficient evidence.
- ▶ Considering the local situation, evidence based on observational studies could be used.
- ▶ A modeling approach might be used to connect a chain of evidence if there is no direct evidence.
- ▶ Basic requirement is needed to be developed for the introduction of new methods for cancer screening considering the balance of evidence and the local situation, particularly disease burden.

Conclusions

- ▶ Cancer screening guidelines in Korea and Japan have been developed based on both scientific evidence and the local situations.
- ▶ Further studies are needed to formulate recommendations considering local situations and weak evidence.